REMARKS

I. REQUEST FOR WITHDRAWAL OF REJECTIONS AND PROMPT ISSUANCE OF NOTICE OF ALLOWANCE

Reconsideration and withdrawal of the rejections of the present application and prompt issuance of a Notice of Allowance are respectfully requested in view of the amendments and remarks herewith, the amendments and remarks and accompanying documents and Declarations previously filed, and the matters discussed during the personal interview with Practice Specialist Elliot, SPE Chan and the Examiner, who are thanked for the courtesies extended.

II. REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, prior to issuance of any paper (other than a Notice of Allowance), an interview, with supervisory review if necessary, is again respectfully requested, especially in view of the amendments and remarks herewith, the amendments and remarks and accompanying documents and Declarations previously filed, and the matters discussed during the personal interview with Practice Specialist Elliot, SPE Chan and the Examiner.

III. THE PATENTABLE CLAIMS

Presented herewith are claims 56-71 and 73-84. Any fee occasioned by this paper or the claims herewith may be charged, or any overpayment in fees credited, to Deposit Account No. 50-0320.

It is submitted that the claims previously pending and the claims presented herewith are patentably distinct from the prior art cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112.

The amendment and presentation herewith of claims is not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather claims are presented simply for clarification and to round out the scope of protection to which Applicants are entitled.

Indeed, it is also noted that claims 56-71 and 73-84 are not considered narrower than previously presented claims; and hence, claims 56-71 and 73-84 are presented without prejudice, without admission, without surrender of subject matter and without any intention of creating any estoppel as to equivalents.

Support for claims 56-71 and 73-84 can be found throughout the present application, including the originally-filed claims and Examples, note, for instance: how the text prior to the Examples teaches that the Examples describe the invention (page 10); how the text prior to the Examples teaches that a fragment of the self-protein is substituted with a foreign T-cell epitope (page 10); how the text prior to the Examples teaches correspondence between the peptide fragment and the peptide containing the T-cell epitope (e.g., pages 5, 8, 9); how the original claims teach that the flanking region is at least 4 amino acids and that the T-cell epitope contains at least 10 or 15 amino acids; how the Examples teach correspondence between the peptide fragment and the peptide containing the T-cell, how the Examples employ T-cell epitopes containing 10 or 15 amino acids; how the Examples teach substitution of an alpha helix, such as an amphiphatic alpha helix; how the Examples teach detoxification by substitution; how the Examples teach eliciting a response that includes an MHC class II response to the T-cell epitope and an autoantibody response in other MHC-haplotypes; how the specification and Examples teach preparing different modified self-proteins which differ with respect to each other by the position of the immunodominant T-cell epitope and then selecting the modified self protein that elicits the desired specific neutralizing effect, and administering the selected modified self-protein, *inter alia*. And attention is also directed to the description of the invention in the "Description of the Prior Art", the "Summary of the Invention", and the "Description of the Preferred Embodiments" (e.g., pages 3-4 teaching that the present invention includes T-cell epitopes substituting fragments of the self protein and preserving secondary and tertiary structure, page 4 teaching that the present invention can include "using the complete [self-] protein for facilitating the broadest possible self epitope sequences", *inter alia*).

Thus, in view of these teachings and those identified in the previously-filed Amendment no new matter is added.

Furthermore, in view of these claim recitations and the claim recitations discussed in the previously-filed Amendment, the presently claimed invention is patentable over the documents of record and cited during the interview, e.g., Russell-Jones and U.S. Patent No. 5,583,202. Simply, the recitations of the instant claims are not taught or suggested by the documents of record, e.g., Russell-Jones and U.S. Patent No. 5,583,202, either individually or in any fair combination.

In particular, there is no teaching or suggestion in the art of: the peptide fragment and T-cell epitope containing fragment being the same length (claim 56), for instance wherein a flanking region on each side of the peptide fragment of 4 amino acids is preserved (claim 63); or the substitution being of an alpha-helix such as an amphiphatic alpha-helix (claims 57-58); or of the peptide fragment and T-cell epitope containing fragment being the same length and comprising 10 or 15 amino acids (claims 59, 60), for instance, wherein a flanking region of 4 amino acids on each side of the peptide fragment is preserved, (claims 64, 65); or of eliciting a response that includes an MHC class II response to the T-cell epitope and an autoantibody response in other MHC-haplotypes (claim 61); or of detoxifying the self-protein, such as wherein the T-cell epitope corresponds in length to the peptide fragment and comprises 10 amino acids (claim 62, 66, 67); or of preparing different modified self-proteins which differ with respect to each other by the position of the immunodominant T-cell epitope and then selecting the modified self protein that elicits the desired specific neutralizing effect, and administering the selected modified self-protein, such as wherein the T-cell epitope contains 15 amino acids (claim 68, 69); or of a method for breaking B-cell autotolerance and inducing earlier and higher antibody titres (claim 70), or of a method for breaking B-cell autotolerance and eliciting an MHC class II response to the T-cell epitope and an autoantibody response in other MHC-haplotypes (claim 71); or the particular recitations of claims 73-84, especially the particular self-proteins of claims 80-84.

Accordingly, the instant invention is not taught or suggested in, and is patentable over, the art.

And reconsideration and withdrawal of the rejections of the application are earnestly solicited.

CONCLUSION

In view of the the amendments and remarks herewith, the amendments and remarks and accompanying documents and Declarations previously filed, and the matters discussed during the personal interview with Practice Specialist Elliot, SPE Chan and the Examiner, who are again thanked for the many courtesies extended during the interview, the application is in condition for allowance.

Favorable reconsideration of the application, reconsideration and withdrawal of the rejections, and prompt issuance of a Notice of Allowance, or another interview with a view towards reaching agreement on allowance, are earnestly solicited.

And again, prior to issuance of any paper other than a Notice of Allowance, the Examiner is respectfully invited and requested to telephonically contact the undersigned so that the Examiner and the undersigned may conduct a further interview, with supervisory review if necessary, with a view towards reaching agreement on allowable subject matter, especially as expediting prosecution and reaching agreement with the Examiner on allowable subject matter are desired.

Respectfully submitted,

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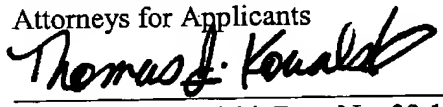

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APPENDIX: MARKED VERSION OF AMENDMENT

It is respectfully requested that the application be amended without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

IN THE CLAIMS

Please amend the claims, as follows, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents:

56. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving tertiary structure of the self-protein] wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length;

whereby, the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

57. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein] wherein the substitution is of an alpha-helix;

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

58. (Amended) The [A] method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, according to claim 57 wherein the alpha helix is an amphiphatic alpha helix [comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving tertiary structure of the self-protein, and said substitution preserving flanking regions comprising at least four amino acids on each side of the peptide fragment;

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken].

59. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises [said substitution preserving tertiary structure of the self-protein, and said substitution preserving flanking regions comprising] at least ten amino acids [on each side of the peptide fragment];

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

60. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises [said substitution preserving tertiary structure of the self-protein, and said substitution preserving flanking regions comprising] at least fifteen amino acids [on each side of the peptide fragment],

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

61. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal[, said substitution preserving tertiary structure of the self-protein],

whereby the modified self-protein elicits antibodies that are against the self-protein; and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes, and B-cell autotolerance to the self-protein is broken.

62. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of

that animal, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified [and] by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving tertiary structure of the self-protein,]

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

63. (Amended) The [A] method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, of claim 56 wherein the substitution preserves [comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein, and said substitution preserving] flanking regions comprising at least four amino acids on each side of the peptide fragment[;

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken].

64. (Amended) The [A] method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, of claim 59 wherein the substitution preserves [comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein, and said substitution preserving] flanking regions comprising at least [ten] four amino acids on each side of the peptide fragment[;

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken].

65. (Amended) [A] The method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, of claim 60 wherein the substitution preserves [comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein, and said substitution preserving] flanking regions comprising at least [fifteen] four amino acids on each side of the peptide fragment[,

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken].

66. (Amended) The [A] method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal of claim 62 wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length[, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least

one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein; and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes, and B-cell autotolerance to the self-protein is broken].

67. (Amended) [A] The method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal of claim 66 wherein the T-cell epitope comprises at least 10 amino acids[, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by being detoxified and by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

68. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising;

preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

[said substitution preserving tertiary structure of the self-protein,] and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken].

69. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising;

preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self- protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

[said substitution preserving secondary and tertiary structure of the self-protein,] and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken, wherein:
the peptide containing at least one immunodominant T-cell epitope comprises at least 15 amino acids.

70. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier

protein or peptide containing T-cell epitopes, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

a. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length [said substitution preserving tertiary structure of the self-protein];

whereby, the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

b. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the substitution is of an amphiphatic alpha helix [said substitution preserving secondary and tertiary structure of the self-protein];

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

c. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises [said substitution preserving tertiary structure of the

self-protein, and said substitution preserving flanking regions comprising] at least [four] ten amino acids [on each side of the peptide fragment];

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

d. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises [said substitution preserving tertiary structure of the self-protein, and said substitution preserving flanking regions comprising] at least [ten] fifteen amino acids [on each side of the peptide fragment];

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

e. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises at least 10 amino acids with [said substitution preserving tertiary structure of the self-protein, and] said substitution preserving flanking regions comprising at least [fifteen] four amino acids on each side of the peptide fragment,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier

protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

f. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal[, said substitution preserving tertiary structure of the self-protein], wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises at least 15 amino acids with said substitution preserving flanking regions comprising at least four amino acids on each side of the peptide fragment,

whereby the modified self-protein elicits antibodies that are against the self-protein earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes; [and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes,] and B-cell autotolerance to the self-protein is broken; or,

g. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified [and] by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving tertiary structure of the self-protein,]

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

h. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified by containing a substitution of [at least one] a peptide fragment of the self-protein

with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein,] and said substitution preserving flanking regions comprising at least four amino acids on each side of the peptide fragment;

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

i. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by <u>being detoxified by</u> containing a substitution of [at least one] <u>a</u> peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein,] <u>wherein said peptide containing at least one immunodominant T-cell epitope comprises at least 10 amino acids</u> and said substitution [preserving] <u>preserves</u> flanking regions comprising at least [ten] <u>four</u> amino acids on each side of the peptide fragment;

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

j. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by <u>being detoxified by</u> containing a substitution of [at least one] <u>a</u> peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein,] <u>wherein the peptide containing at least one immunodominant T-cell epitope comprises at least 15 amino acids</u> and said substitution [preserving] <u>preserves</u> flanking regions comprising at least [fifteen] <u>four</u> amino acids on each side of the peptide fragment,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

[k. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes; and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes, and B-cell autotolerance to the self-protein is broken; or,

1. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by being detoxified and by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

m. preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

said substitution preserving tertiary structure of the self-protein, and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

n. preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

said substitution preserving secondary and tertiary structure of the self-protein, and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken].

71. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, inducing antibody production in the animal against the self-protein of that animal, and eliciting an immune response in the animal which includes an MHC class II immune response as to an immunodominant T-cell epitope which is foreign to the animal and an autoantibody response in other MHC-haplotypes, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

[a.] the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing the immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving tertiary structure of the self-protein,]

whereby the modified self-protein elicits antibodies that are against the self-protein; and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes, and B-cell autotolerance to the self-protein is broken[; or

b. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing the immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein; and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes, and B-cell autotolerance to the self-protein is broken].

73. (Amended) The method of any one of claims 56-[72] 71 wherein the modified self-protein is a recombinant modified self-protein.

74. (Amended) The method of any one of claims 56-[72] 71 wherein the self-protein is tumor necrosis factor alpha (TNF-α), tumor [nucrosis] necrosis factor beta (TNF-β), gamma interferon (γ-interferon), interleukin 1 (IL-1) or immune globulin (IgE).

75. (Not Amended) The method of claim 73 wherein the self-protein is tumor necrosis factor alpha (TNF-α), tumor [nucrosis] necrosis factor beta (TNF-β), gamma interferon (γ-interferon), interleukin 1 (IL-1) or immune globulin (IgE).

76. (Amended) The method of any one of claims 56-[72] 71 wherein the administering includes administering an adjuvant.

77. (Not Amended) The method of claim 76 wherein the adjuvant comprises calcium phosphate, saponin, quil A or a biodegradable polymer.

78. (Not Amended) The method of claim 73 wherein the administering includes an adjuvant.

79. (Not Amended) The method of claim 75 wherein the administering includes an adjuvant.

Please add the following new claims, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents:

--80. (New) The method of claim 79 wherein the self-protein is tumor necrosis factor alpha (TNF-α).

81. (New) The method of claim 79 wherein the self-protein is tumor nucrosis factor beta (TNF-β).

82. (New) The method of claim 79 wherein the self-protein is gamma interferon (γ-interferon).

83. (New) The method of claim 79 wherein the self-protein is interleukin 1 (IL-1).

84. (New) The method of claim 79 wherein the self-protein is immune globulin (IgE).--

Please cancel claim 72, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.